K140029

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510(K) SUMMARY

The following information is provided as required by 21 CFR § 807.87 for Quidel Corporation 510(k) premarket notification for the AmpliVue® HSV 1+2 Assay. In response to the Safe Medical Devices Act of 1990, the following is a summary of the information upon which the substantial equivalence determination is based.

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Date of preparation of 510(k) summary:

December 30, 2013

Device Name:

Trade name:	AmpliVue® HSV 1+2 Assay
Classification name:	Herpes Simplex Virus Nucleic Acid Amplification Assay
Product Code:	OQO
Class:	II
Regulation:	21 CFR 866.3305 Herpes simplex virus serological assays
Panel:	Microbiology (83)

Substantial Equivalency

The AmpliVue® HSV 1+2 Assay is substantially equivalent in principle to the currently marketed IsoAmp® HSV Assay for the direct, qualitative detection of Herpes Simplex Virus 1 (HSV-1) and

Herpes Simplex Virus 2 (HSV-2) nucleic acids. The clinical performance of the AmpliVue™ HSV 1+2 Assay for the differentiation of Herpes Simplex Virus 1 (HSV-1) and Herpes Simplex Virus 2 (HSV-2) nucleic acids was compared with the ELVIS® HSV ID and D³ Typing Test System which is the gold standard/reference method *i.e.*, cell culture using an enzyme linked virus inducible system.

Comparison of New Device with Predicate Device

Features	AmpliVue® HSV 1+2 Assay Quidel Corporation	IsoAmp® HSV Assay BioHelix Corporation (K111951)
Intended Use	The AmpliVue® HSV 1+2 Assay is an *in vitro* diagnostic test for the direct, qualitative detection and differentiation of Herpes Simplex Virus 1 (HSV-1) and Herpes Simplex Virus 2 (HSV-2) DNA in cutaneous or mucocutaneous lesion specimens from symptomatic patients. The test is intended for use as an aid in diagnosis of HSV infection in symptomatic patients. ***Warning***: The AmpliVue HSV 1+2 Assay is not FDA cleared for use with cerebrospinal fluid (CSF). The assay is not intended for prenatal screening.	The IsoAmp® HSV Assay is an *in vitro* diagnostic test for the direct, qualitative detection of the Herpes Simplex Virus (HSV-1 + HSV-2) DNA in male and female genital and oral lesions. The test is intended for use as an aid in diagnosis of HSV infection in symptomatic patients. ***Warning***: The IsoAmp®HSV Assay is not FDA cleared for use with cerebrospinal fluid (CSF). The assay does not provide specific typing information to differentiate HSV-1 and HSV-2. The assay is not intended to be used for prenatal screening.
Assay Results	Qualitative	Qualitative
Detection of HSV-1 and HSV-2	Yes	Yes
Typing of HSV-1 and HSV-2	Yes	No
Methodology	HDA (Helicase-Dependent Amplification)	HDA (Helicase-Dependent Amplification)
Packaging	Supplied as a kit; 16 tests per kit 1. Amplification-related Kit Components (ARKC) 2. Non-amplification related Kit Components (NKC)	The product is supplied as two separate labeled boxes. 1. Amplification-related Kit Components (ARKC) 2. Non-amplification related Kit Components (NKC)
Kit Reagent Storage Conditions	ARKC: 2°C to 8°C NKC: 2°C to 30°C	ARKC: <-15°C NKC: 15-30°C

Indications for Use and Intended Use

The AmpliVue® HSV 1+2 Assay is an *in vitro* diagnostic test for the direct, qualitative detection and differentiation of Herpes Simplex Virus 1 (HSV-1) and Herpes Simplex Virus 2 (HSV-2) DNA in cutaneous or mucocutaneous lesion specimens from symptomatic patients. The test is intended for use as an aid in diagnosis of HSV infection in symptomatic patients.

***Warning*: The AmpliVue HSV 1+2 Assay is not FDA cleared for use with cerebrospinal fluid (CSF). The assay is not intended for prenatal screening.**

Methodology

The AmpliVue® HSV 1+2 Assay consists of three major steps: 1) specimen preparation, 2) isothermal Helicase-Dependent Amplification (HDA) of target amplicons specific to HSV-1 and HSV-2, and 3) detection of the amplified DNA by target-specific hybridization probes via a colorimetric reaction on a lateral-flow strip which is embedded in a self-contained disposable cassette to prevent amplicon contamination.

Specimen preparation involves one simple dilution step in which specimens in viral transport medium are diluted 80-fold in Dilution Tubes.

The diluted samples are transferred into a 0.2 mL Amplification Tube containing lyophilized HDA reagents. Incubation at 64°C for 45 minutes results in the release of the HSV DNA and subsequent isothermal amplification of the target sequence. The amplified DNA is detected by a set of specific detection probes included in the Amplification Tube: HSV-1 target hybridizes to two specific probes labeled with Biotin (BioTEG) and Digoxigenin (DIG) and HSV-2 target hybridizes to two specific probes labeled with Biotin (BioTEG) and Fluorescein isothiocyanate (FITC). A competitive internal control (IC) is included in the Amplification Tube to monitor inhibitory substances in clinical samples, reagent failure or device failure. The IC target is amplified by HSV-2 specific primers and hybridizes to the biotin-labeled HSV-2 probe and a IC specific probe labeled with 2,4-dinitrophenyl (DNP-TEG).

Detection of the amplified DNA with specific probes is achieved by Type III BEStTM cassettes. The self-contained Type III BEStTM cassettes carry lateral-flow DNA detection strips coated with anti-DNP antibodies (C line), anti-DIG antibodies (T1 line) and anti-FITC antibodies (T2 line). HSV-1 amplicon with BioTEG and DIG-labeled probes is captured by anti-DIG antibodies at the T1-Line and HSV-2 amplicon with BioTEG and FITC-labeled probes is captured by anti-FITC antibodies at the T2-Line, while the IC amplicon with BioTEG and DNP-labeled probes is captured by anti-DNP antibodies at the C-Line. The Biotin in the amplicon-probe complexes captures the streptavidin-conjugated color particles for visualization and the test result is shown as colored lines that are visually read.

A positive result for HSV-1 (detection of HSV-1 DNA) is reported when the T1 line is visible through the detection window of the cassette, while a positive result for HSV-2 (detection of HSV-2 DNA) is reported when the T2 line is visible through the detection window of the cassette. A positive result for both HSV-1 and HSV-2 (detection of both HSV-1 and HSV-2 DNA) is reported when both the T1 line and the T2 line are visible through the detection window

of the cassette. A negative result (no detection of HSV-1 or HSV-2 DNA) is reported when only the C line is displayed. The assay result is regarded as invalid when the T1 line, T2 line and C line are not present and the assay should be repeated.

Analytical Performance

Reproducibility

The reproducibility of the AmpliVue® HSV 1+2 Assay was evaluated at three test sites using a panel consisting of four panel members: HSV 1+2 High Negative; HSV-1 Low Positive; HSV-2 Low Positive; and HSV 1+2 Moderate Positive members. The HSV-1 Low Positive member served as a HSV-2 Negative member and the HSV-2 Low Positive member served as a HSV-1 Negative member. The panel members were prepared in HSV Negative Matrix that consisted of a pool of HSV negative cheek swabs in M4 medium. HSV Negative Matrix was spiked with quantified HSV 1 and 2 viral stocks at pre-determined $TCID_{50}$ concentrations. The HSV viral stock was diluted in the HSV Negative Matrix to three (3) different concentration levels, defined as High Negative member (0.3 x LoD), Low Positive member (1 x LoD) and Moderate Positive member (3 x LoD level).

Each run tested the four member panel of four members in triplicate and also included three each of HSV-1 + HSV-2 positive control, and negative control. Two (2) operators per test site each carried out one run of the four member panel plus controls per test day for five (5) days using one lot of the AmpliVue® HSV 1+2 Assay.

Results of the Reproducibility study for the AmpliVue® HSV 1+2 Assay performed at three sites are presented in the tables below.

Reproducibility Study Summary for HSV-1

Category	Site						Rate of Detection	Overall Percent Agreement	95% Confidence Interval
	Site #1		Site #2		Site #3				
	Rate of Detection	Percent Agreement	Rate of Detection	Percent Agreement	Rate of Detection	Percent Agreement			
HSV 1+2 High Negative	16/30	47%	9/30	70%	20/30	33%	45/90	50%	40% - 60%
HSV-1 Low Positive	30/30	100%	29/30	97%	30/30	100%	89/90	99%	94% - 100%
HSV 1+2 Moderate Positive	30/30	100%	30/30	100%	30/30	100%	90/90	100%	96% - 100%
HSV-2 Low	0/30	100%	0/30	100%	0/30	100%	0/90	100%	96% - 100%

Reproducibility Study Summary for HSV-1

Category	Site						Rate of Detection	Overall Percent Agreement	95% Confidence Interval
	Site #1		Site #2		Site #3				
	Rate of Detection	Percent Agreement	Rate of Detection	Percent Agreement	Rate of Detection	Percent Agreement			
Positive									
HSV-1+2 Positive Control	30/30	100%	30/30	100%	30/30	100%	90/90	100%	96% - 100%
Negative Control	0/30	100%	0/30	100%	0/30	100%	0/90	100%	96% - 100%

Reproducibility Study Summary for HSV-2

Category	Site						Rate of Detection	Overall Percent Agreement	95% Confidence Interval
	Site #1		Site #2		Site #3				
	Rate of Detection	Percent Agreement	Rate of Detection	Percent Agreement	Rate of Detection	Percent Agreement			
HSV1+-2 High Negative	20/30	33%	17/30	43%	13/30	57%	50/90	44%	35% - 55%
HSV-2 Low Positive	30/30	100%	30/30	100%	30/30	100%	90/90	100%	96% - 100%
HSV 1+-2 Moderate Positive	30/30	100%	30/30	100%	30/30	100%	90/90	100%	96% - 100%
HSV-1 Low Positive	0/30	100%	0/30	100%	0/30	100%	0/90	100%	96% - 100%
HSV-1+2 Positive Control	30/30	100%	30/30	100%	30/30	100%	90/90	100%	96% - 100%
Negative Control	0/30	100%	0/30	100%	0/30	100%	0/90	100%	96% - 100%

Repeatability

For the Precision/Within Laboratory Repeatability study, a blinded four-member panel consisting of medium positive and low positive, high negative 3x, 1x, ≤0.3x LoD, respectively) and negative HSV-1 and HSV-2 samples were tested in triplicate by two (2) operators, twice a day (2X) for twelve (12) days on all three instruments (triplicate testing x 2 operators x 12 days = 72 results per level for each virus). Positive and negative controls were run in triplicate with each test run. Results of the Precision/Within Laboratory Repeatability study for the AmpliVue® HSV 1+2 Assay performed are presented in the tables below.

Repeatability Study Summary for HSV-1

Category	Rate of Detection	Overall Percent Agreement	95% Confidence Interval
HSV-1+2 High Negative	35/72	51%	40 – 63%
HSV-1 Low Positive	72/72	100%	95 – 100%
HSV 1+2 Moderate Positive	72/72	100%	95 – 100%
HSV-1 Negative Sample	0/72	100%	95 – 100%
HSV-1+2 Positive Control	72/72	100%	95 – 100%
Assay Negative Control	0/72	100%	95 – 100%

Repeatability Study Summary for HSV-2

Category	Rate of Detection	Overall Percent Agreement	95% Confidence Interval
HSV-1+2 High Negative	43/72	40%	30 – 52%
HSV-2 Low Positive	72/72	100%	95 – 100%
HSV-1+2 Moderate Positive	72/72	100%	95 – 100%
HSV-2 Negative Sample	0/72	100%	95 – 100%
HSV-1+2 Positive Control	72/72	100%	95 – 100%
Assay Negative Control	0/72	100%	95 – 100%

Level of Detection (LoD)

A Limit of Detection (LoD) study was performed to evaluate the analytical sensitivity of AmpliVue HSV 1+2 Assay using a two representative viral strains of HSV-1 (McIntyre & HF) and two representative strains of HSV-2 (G & MS). Quantified ($TCID_{50}$/mL) cultures of the HSV-1 and HSV-2 strains were serially diluted to five (5) concentrations in HSV-negative matrix pools and tested in replicates of ten (10) on three reagent lots. The observed LoD of a HSV strain was determined as the lowest concentration level that had a positivity rate of ≥95%. The observed limit of detection of HSV-1 and HSV-2 were determined to be 1.1×10^5 $TCID_{50}$/mL and 1.1×10^4 $TCID_{50}$/mL, respectively.

Results obtained with each HSV LoD panels:

Strain	Concentration $TCID_{50}$/mL	Positive/Total	Positivity rate	95% CI	
HSV-1 McIntyre	1.00×10^6	30/30	100.0%	88.65%	100.00%
	3.33×10^6	30/30	100.0%	88.65%	100.00%
	1.1×10^5	30/30	100.0%	88.65%	100.00%
	3.70×10^4	24/30	80.0%	62.69%	90.50%
	1.23×10^4	8/30	26.7%	14.18%	44.45%
HSV-1 HF	1.00×10^6	30/30	100.0%	88.65%	100.00%
	3.33×10^5	30/30	100.0%	88.65%	100.00%
	1.11×10^5	30/30	100.0%	88.65%	100.00%
	3.70×10^4	23/30	76.7%	59.07%	88.21%
	1.23×10^4	9/10	30.0%	16.66%	47.88%
HSV-2 G	1.00×10^5	30/30	100.0%	88.65%	100.00%
	3.33×10^4	30/30	100.0%	88.65%	100.00%
	1.11×10^4	29/30	100.0%	88.30%	100.00%
	3.70×10^3	28/30	93.3%	78.68%	98.15%
	1.23×10^3	24/30	73.3%	55.55%	85.82%
HSV-2 MS	1.00×10^5	30/30	100.0%	88.65%	100.00%
	3.33×10^4	30/30	100.0%	88.65%	100.00%
	1.11×10^4	30/30	100.0%	88.65%	100.00%
	3.70×10^3	30/30	100.0%	88.65%	100.00%
	1.23×10^3	27/30	90.0%	74.38%	96.54%

The LoD was confirmed with the same two (2) HSV-1 and two (2) HSV-2 reference strains diluted to the observed LoD and tested with twenty (20) replicates using three (3) lots of AmpliVue HSV 1+2 Assay. Since all HSV-1 and HSV-2 strains show positivity rates of ≥95% with all three (3) validation lots, the observed LoD is confirmed for both HSV-1 and HSV-2. In addition, twenty (20) HSV-1 and twenty (20) HSV-2 clinical isolates were cultured and quantified in $TCID_{50}$/mL. Each isolate was diluted to the corresponding LoD in HSV-negative matrix and tested in triplicate. AmpliVue HSV 1+2 Assay was able to detect all 20 HSV-1 and 20 HSV-2 clinical isolates.

Assay LoD: The final assay LoD claim is 1.1×10^5 $TCID_{50}$/mL for HSV-1 and 1.1×10^4 $TCID_{50}$/mL for HSV-2.

Analytical Specificity/Cross-Reactivity

A study was performed to evaluate the performance of the AmpliVue® HSV 1+2 Assay in the presence of eighty-nine (89) microorganisms that might be found in lesion specimens. The panel members were obtained from suppliers as purified genomic DNA (GD) or quantified cultures (QC), or prepared in house (IHC) by growing each organism and quantifying the culture. Each potentially interfering or cross-reactive microorganism was tested in three (3) replicates the presence of negative matrix or 3x LoD HSV-1 and HSV-2. Clinically relevant levels of viruses and bacteria are typically 10^6cfu/ml or higher for bacteria and 10^5pfu/ml or higher for viruses. Purified and quantified DNA or RNA was used for seven (7) of the microorganisms. For these microorganisms 10^6 copies per ml (cp/ml) or higher was used.

None of the eighty-nine (89) microorganisms that might be found in lesion specimens interfere or cross-react with the assay.

Cross Reactivity Panel

Microorganism	Member Type (GD, QC , IHC)	Test concentration
Bacteria (N=52)		
Acholeplasma laidlawi PG8	QC	7.1 x 10^6 cfu/mL
Acinetobacter calcoaceticus	QC	9.80 x 10^6 cfu/mL
Acinetobacter lwoffi	IHC	4.55 x 10^6 cfu/mL
Bacteroides fragilis Z029	QC	8.8 x 10^6 cfu/mL
Bordetella bronchiseptica	QC	1.17 x 10^6 cfu/mL
Bordetella pertussis E431	QC	1.73 x 10^6 cfu/mL
Chlamydia trachomatis VR-347	QC	3.00 x 10^6 cfu/mL
Chlamydia trachomatis D-UW3	QC	7.83 x 10^7 IFU/mL
Chlamydia trachomatis LGV-II 434 DNA	GD	1.5 x 10^7 cp/mL
Chlamydophila pneumoniae DNA	GD	1.6 x 10^6 cp/mL
Clostridium difficile NAP1	QC	6.77 x 10^6 cfu/mL
Clostridium perfringens Type A	QC	1.06 x 10^6 cfu/mL
Corynebacterium diphtheriae	QC	3.44 x 10^6 cfu/mL
Enterobacter cloacae Z101	QC	5.70 x 10^6 cfu/mL
Enterococcus faecalis VSE	QC	8.60 x 10^6 cfu/mL
Escherichia coli ATCC 43895	QC	1.13 x 10^6 cfu/mL
Fusobacterium nucleatum	IHC	8.05 x 10^6 cfu/mL
Gardnerella vaginalis	QC	1.20 x 10^6 cfu/mL
Haemophilis influenzae type A	QC	4.00 x 10^6 cfu/mL
Haemophilus ducreyi Class I DNA	GD	2.97 x 10^6 cp/mL

Microorganism	Member Type (GD, QC , IHC)	Test concentration
Klebsiella pneumoniae	QC	9.75 x 10^6 cfu/mL
Lactobacillus acidophilus Z048	QC	2.00 x 10^6 cfu/mL
Legionella pneumophila	QC	1.42 x 10^6 cfu/mL
Mobiluncus curtisii V125 [DSM 2711] ATCC 43063	QC	3.2 x 10^6 cfu/mL
Mobiluncus mulieris ATCC 35240	QC	1.76 x 10^6 cfu/mL
Moraxella cartarrhalis Ne11	QC	9.90 x 10^6 cfu/mL
Mycoplasma hominis LBD-4	QC	1.30 x 10^6 cfu/mL
Mycoplasma hyorhinis BTS-7	QC	6.6 x 10^6 cfu/mL
Mycoplasma orale CH 19299	QC	3.08 x 10^6 cfu/mL
Mycoplasma pneumoniae M129	QC	3.16 x 10^6 CCU/mL
Mycoplasma salivarium H110	QC	1.67 x 10^6 cfu/mL
Neisseria gonorrhoeae Z017	QC	5.73 x 10^6 cfu/mL
Neisseria meningitidis SerogroupA	QC	7.07 x 10^6 cfu/mL
Prevotella melaninogenica ATCC 25845	QC	7.3 x 10^6 cfu/mL
Proteus mirabilis	QC	1.19 x 10^6 cfu/mL
Pseudomonas aeruginosa	QC	1.32 x 10^6 cfu/mL
Salmonella enteriditis	QC	5.40 x 10^6 cfu/mL
Salmonella typhimurium	QC	4.60 x 10^6 cfu/mL
Staphylococcus aureus MRSA	IHC	7.52 x 10^6 cfu/mL
Staphylococcus aureus MSSA	IHC	7.02 x 10^6 cfu/mL
Staphylococcus epidermidis MRSE	IHC	1.75 x 10^6 cfu/mL
Staphylococcus saprophyticus	QC	3.00 x 10^6 cfu/mL
Streptococcus agalactiae	QC	2.20 x 10^6 cfu/mL
Streptococcus mitis	QC	2.43 x 10^6 cfu/mL
Streptococcus mutans Z072	QC	1.17 x 10^6 cfu/mL
Streptococcus pneumonia	QC	2.8 x 10^6 cfu/mL
Streptococcus pyogenes ATCC 9898	QC	6.38 x 10^6 cfu/mL
Streptococcus salivarius	IHC	2.75 x 10^6 cfu/mL
Toxoplasma gondii	QC	6.6 x 10^6 tachyzoties/mL
Treponema pallidum Nichols	QC	2.0 x 10^6 Tp/mL
Trichomonas vaginalis Z070	QC	1.65 x 10^6 trophzoites/mL
Ureaplasma uralyticum NCTC 10177 DNA	GD	1.23 x 10^6 cp/mL
Yeast (N=7)		
Candida albicans	QC	2.00 x 10^6 cfu/mL

Microorganism	Member Type (GD, QC , IHC)	Test concentration
Candida glabrata Z007	QC	9.73 x 10^6 cfu/mL
Candida guilliermondii Z008	QC	9.96 x 10^6 cfu/mL
Candida krusei Z009	QC	5.33 x 10^6 cfu/mL
Candida lusitaniae Z010	QC	6.56 x 10^6 cfu/mL
Candida parapsilosis Z011	QC	1.24 x 10^6 cfu/mL
Candida tropicalis Z012	QC	1.0 x 10^6 cfu/mL
Virus (N=30)		
Influenza A/Mexico/4108/2009 H1N1	QC	4.08 x 10^6 $TCID_{50}$/mL
Adenovirus 2	QC	1.02 x 10^5 $TCID_{50}$/mL
Adenovirus 7 VR-7	QC	1.58 x 10^5 $TCID_{50}$/mL
Coronavirus OC43 VR-1558	QC	2.42 x 10^5 $TCID_{50}$/mL
Coxsackievirus B4	QC	1.08 x 10^5 $TCID_{50}$/mL
Cytomegalovirus AD-169	QC	9.55 x 10^5 $TCID_{50}$/mL
Echovirus 11 ODH-37285	QC	2.14 x 10^5 $TCID_{50}$/mL
Enterovirus Type 71	QC	1.00 x 10^5 $TCID_{50}$/mL
Epstein-Barr Virus B95-8	GD	2.22 x 10^5 cp/mL
Influenza B Hong Kong VR-791	QC	9.53 x 10^6 $TCID_{50}$/mL
Hepatitis B Virus	QC	3.44 x 10^5 IU/mL
Hepatitis C Virus	QC	7.58 x 10^5 IU/mL
HHV-8	QC	1.26 x 10^5 $TCID_{50}$/mL
HIV-1 Subtype B RNA	GD	1.14 x 10^5 cp/mL
hMPV (Italy) A1	QC	3.66 x 10^5 $TCID_{50}$/mL
Human Herpes 6 virus Z29 strain	QC	1.95 x 10^5 $TCID_{50}$/mL
Human Herpes 7 virus SB strain	QC	1.15 x 10^5 $TCID_{50}$/mL
Human papilloma virus 16 DNA	GD	4.3 x 10^5 cp/mL
Human papilloma virus 18 DNA	GD	1.8 – 3.6 x 10^5 cp/mL
Measles virus	QC	1.95 x 10^5 $TCID_{50}$/mL
Mumps virus	QC	5.89 x 10^5 $TCID_{50}$/mL
Parainfluenza Type 1 #2	QC	3.97 x 10^5 $TCID_{50}$/mL
Parainfluenza Type 2	QC	3.15 x 10^5 $TCID_{50}$/mL
Parainfluenza Type 3 NY14	QC	2.36 x 10^5 $TCID_{50}$/mL
Parainfluenza Type 4B VR-1377	QC	1.37 x 10^5 $TCID_{50}$/mL
RSV A Long VR-26	QC	4.36 x 10^4 $TCID_{50}$/mL
RSV B Washington VR-1401	QC	3.43 x 10^5 $TCID_{50}$/mL
Rubella virus	QC	4.17 x 10^5 $TCID_{50}$/mL
Simian Virus type 40 Pa-57 ATCC strain VR-	QC	3.16 x 10^5 $TCID_{50}$/mL

Microorganism	Member Type (GD, QC , IHC)	Test concentration
239		
VZV DNA	GD	1.5 x 10^5 cp/mL

Interfering Substances

This study was performed to evaluate potential interference with AmpliVue HSV 1+2 Assay with a panel of thirty-three (33) substances and five different viral transport media and microorganisms from cross reactivity panel that may be present in clinical specimens.

The study was carried out in the presence of HSV-1 and HSV-2 at 3 x LoD to evaluate potential interference to the detection of the HSV target. The study was also carried out in the absence of HSV to evaluate potential interference to the detection of internal control of AmpliVue HSV 1+2 Assay. Each potential interfering substance was tested in triplicate.

Interfering Substances

The analytical performance of AmpliVue HSV 1+2 Assay was characterized in the presence of interfering substances at potentially highest ("the worst case") concentrations to evaluate the susceptibility of the HSV assay to interference. By "worst case," each interfering substance was introduced into the assay by directly wetting a clean, dry Remel M4 kit swab with the substance and placing the swab directly in transport media. Calculated concentrations are based on an estimated volume of 200µL of substance introduced by the swab. Each panel member was tested in triplicate spiked with HSV-1 HF and HSV-2 G strains separately at 3 x LoD. The panel was also tested in triplicate in the absence of HSV transport media to see if the potentially interfering substances interfere with the detection of the internal control. No interference was observed in the presence of the potential interfering substances tested.

Interfering Substance Panel

Substance	Test conc.
Seminal Fluid	7%
Cornstarch	1.25 mg/mL
Acetamidophenol	5 mg/mL
Feces	7%
Acetylsalicylic Acid	10 mg/mL
Chlorpheniramine	5 mg/mL
Dextromethorphan	10 mg/mL
Whole blood with EDTA	7%
Female Urine	7%
Male Urine	7%
Acyclovir (Acycloguanosine)	7 mg/mL

Substance	Test conc.
Albumin	3.3 mg/mL
Casein	7 mg/mL
K-Y Brand Jelly	7%
Douche	7%
Monistat 1	7%
Monistat 3	7%
Tioconazole 1	7%
Preparation H	7%
Lanacane	7%
Listerine	7%
Abreva	7%
Carmex Cold Sore Lip Balm	7%
Releev cold sore treatment	7%
Crest	7%
Mucin (Bovine Submaxillary Gland, type I-S)	60 µg/mL
Buffy coat	7%
YeastGard	7%
Vagisil Crème	7%
Lip clear Lysine	7%
Clotrimazole 3 Vaginal Cream	7%
Balneol Hygienic Cleansing Lotion	7%
Ortho Options Gynol II Extra Strength Vaginal Contraceptive Jelly	7%

Viral Transport Media

The performance of the AmpliVue HSV 1+2 Assay was assessed with Remel M5, Remel M4RT, Bartels VTM, and BD Universal Viral Transport (UVT)/ Copan UTM. (Remel M4 had previously been assessed and found to not interfere with the assay). Each medium was tested after spiking with HSV-1 HF and HSV-2 G strain to a final concentration of approximately 3 x LoD to determine if the viral transport media interferes with the detection of HSV targets in positive samples. The media were tested in the absence of HSV-1 and HSV-2 (medium only) to see if the viral transport media interfere with the detection of the internal control in negative samples.

There was no interference observed with the Remel M4RT, Remel M5, Bartels VTM, and BD UVT/Copan UTM media for the detection of HSV-1 and HSV- 2 target or the internal control. Remel M4RT, Remel M5, Bartels VTM, and BD UVT/Copan UTM did not interfere with the detection of HSV-1 and HSV-2 target or the internal control.

Cross-Reactivity Panel Members

The performance of the AmpliVue HSV 1+2 Assay was characterized by testing the eighty-nine (89) microorganisms that were evaluated for analytical specificity and cross reactivity in the presence of HSV-1 HF and HSV-2 G at 3 x LoD separately to see if the presence of these organisms interferes with the detection of HSV targets. Each panel member was tested in triplicate. None of the cross reactivity panel members interfered with the detection of HSV-1 and HSV-2 targets.

Specimen Stability

A study was performed to confirm the stability of HSV-1 and HSV-2 in viral transport media in accordance with recommended storage and handling specifications of each medium tested. The five media described above were spiked with HSV-1 or HSV-2 at 3 x LoD and stored at 2 - 8°C or -70°C. The media was tested by AmpliVue HSV 1+2 Assay at multiple time points. Based on this study at 3x LoD, HSV-1 and HSV-2 are stable in all five (5) media for 7 days at 2 - 8°C, and for 34 days at -70°C.

Competitive Inhibition

The performance of the AmpliVue HSV 1+2 Assay was assessed for competitive interference using simulated samples in two studies mimicking co-infections. The first study used simulated samples with one target at a concentration near the LoD (3 x LoD) and the other target at higher concentrations (30x LoD to 3000 x LoD). The second study used simulated samples that had equal concentrations of HSV-1 virus and HSV-2 virus (3 x LoD to 3000 x LoD).

In the first study competitive inhibition was not observed with simulated samples containing one target at a concentration near the LoD (3 x LoD) and the other target at up to 300 x LoD. However, competitive inhibition was observed for both HSV-1 and HSV-2 with simulated samples containing one target at a concentration near the LoD (3 x LoD) and the other target at 3000 x LoD.

In the second study competitive inhibition was not observed with simulated samples containing equal concentrations of HSV-1 virus and HSV-2 virus, from 3 x LoD to 3000 x LoD.

Carry-Over and Cross Contamination

Test results confirm that carry-over and cross contamination does not occur with AmpliVue HSV 1+2 Assay. High HSV-1 (HSV-2) positive samples were tested in series alternating with negative samples. In order to challenge the device, cultured and quantified viral stock served as high positive sample. HSV-1 HF (7.96×10^8 $TCID_{50}$/mL) and HSV-2 G (2.27×10^7 $TCID_{50}$/mL) viral stocks were used directly without dilution, for the highest concentration available. Remel M4 viral transport media was used as negative sample. Ten (10) replicates of negative sample together with assay controls were run by two (2) operators to confirm that negative samples (Remel M4 viral transport media) generate a negative result 100% of the time. Five (5) replicates of high-concentration positive and negative samples were tested in a series, alternating sample types. All HSV-1 and HSV-2 high positive samples gave positive results and all the negative samples gave HSV negative results.

Expected Results

The prevalence of HSV-1 and HSV-2 with the AmpliVue® HSV 1 + 2 Assay in cutaneous (skin lesion, genital - penis), or mucocutaneous (anorectal, genital – vaginal/cervical, nares, ocular, oral lesion and urethral) was estimated for the one thousand three hundred forty-three (1343) specimens with valid AmpliVue® HSV 1 + 2 Assay results. Seven of 1343 specimens were not included in the performance analysis due to contamination or invalid data by reference method.

The prevalence of HSV-1 and HSV-2 with the AmpliVue® HSV 1 + 2 Assay was calculated for the combined sites based on the age of the patient and the specific source of specimen and are presented below.

Combined Study – Cutaneous Prevalence by Age						
	HSV- 1			**HSV-2**		
Age	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence
≤ 5 years	37	2	5.4%	37	1	2.7%
6 to 21 years	68	13	19.1%	68	6	8.8%
22 to 59 years	225	20	8.9%	225	49	21.8%
≥ 60 years	70	5	7.1%	70	18	25.7%
	Percent	**95% CI**		**Percent**	**95% CI**	
Positive Predictive Value	76.9%	88.6% to 100%		79.5%	68.8% to 87.1%	
Negative Predictive Value	100%	94.6% to 98.5%		99.7%	98.3% to 99.9%	

Combined Study – Cutaneous Prevalence by Specific Source						
	HSV- 1			**HSV-2**		
Source	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence
Skin lesion	271	27	10.0%	271	48	17.7%
Genital - penis	129	13	19.1%	129	26	20.2%

Combined Study – Mucocutaneous Prevalence by Age						
	HSV- 1			**HSV-2**		
Age	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence
≤ 5 years	39	10	25.6%	39	1	2.6%
6 to 21 years	190	42	22.1%	190	34	17.9%
22 to 59 years	606	104	17.2%	606	132	21.8%
≥ 60 years	107	16	15.0%	107	17	15.9%
Not provided	1	1	100%	1	0	0%
	Percent	**95% CI**		**Percent**	**95% CI**	
Positive Predictive Value	87.1%	81.3% to 91.3%		81.8%	75.5% to 86.7%	
Negative Predictive Value	98.7%	97.5% to 99.3%		99.5%	98.6% to 99.8%	

Combined Study – Mucocutaneous Prevalence by Specific Source						
	HSV- 1			HSV-2		
Source	Total #	Total Positive	Prevalence	Total #	Total Positive	Prevalence
Anorectal	35	2	5.7%	35	8	22.9%
Genital – vaginal/cervical	691	109	15.9%	691	168	24.3%
Nasal	16	5	31.3%	16	2	12.5%
Ocular	18	3	16.7%	18	1	5.6%
Oral lesion	165	54	32.7%	165	2	1.2%
Urethral	18	0	N/A	18	3	16.7%

Clinical Performance

The performance of the AmpliVue® HSV 1 + 2 Assay was evaluated at five geographically diverse locations within the United States. A total of one thousand three hundred fifty-five (1355) specimens from symptomatic male and female patients were tested. Patient population ranged from ≤ 5 years to ≥ 60 years. The swab specimens have been categorized as cutaneous (skin lesion, genital - penis), or mucocutaneous (anorectal, genital – vaginal/cervical, nares, ocular, oral lesion and urethral). Nineteen (19) tests were considered invalid and were removed from the performance analysis.

The reference ELVIS viral culture used in this study was unable to detect co-infected specimens. Due to this, if a specimen was positive for HSV-2 it was removed from the calculation of the HSV-1 clinical performance. Two hundred eleven (211) specimens identified as HSV-2 positive by ELVIS have been removed from the initial one thousand three hundred thirty-six (1336) specimens. The data below is for the remaining one thousand one hundred twenty-five (1125) specimens.

Combined Sites – HSV-1 Cutaneous Lesions (N=340)								
		Reference Method					95% CI	
		POS	NEG	Total	Sensitivity	100%	88.6%	100%
AmpliVue HSV 1+2 Assay	POS	30	9	39	Specificity	97.1%	94.6%	98.5%
	NEG	0	301	301				
	Total	30	310	340				

Combined Sites – HSV-1 Mucocutaneous Lesions (N=785)								
	Reference Method						95% CI	
		POS	NEG	Total	Sensitivity	94.9%	90.3%	97.4%
AmpliVue HSV 1+2 Assay	POS	149	22	171	Specificity	96.5%	94.8%	97.7%
	NEG	8	606	614				
	Total	157	628	785				

The table below details the HSV-2 results for the one thousand three hundred thirty-six (1336) specimens.

Combined Sites – HSV-2 Cutaneous Lesions (N=399)								
	Reference Method						95% CI	
		POS	NEG	Total	Sensitivity	98.3%	91.0%	99.7%
AmpliVue HSV 1+2 Assay	POS	58	15	73	Specificity	95.6%	92.8%	97.3%
	NEG	1	325	326				
	Total	59	340	399				

Combined Sites – HSV-2 Mucocutaneous Lesions (N=937)								
	Reference Method						95% CI	
		POS	NEG	Total	Sensitivity	97.4%	93.4%	99.0%
AmpliVue HSV 1+2 Assay	POS	148	33	181	Specificity	95.8%	94.2%	97.0%
	NEG	4	752	756				
	Total	152	785	937				

Statement of Performance

The results of the analytical and clinical performance studies submitted in this pre-market notification are complete and demonstrate that the AmpliVue® HSV 1+2 Assay is substantially equivalent to the predicate device. The AmpliVue® HSV 1+2 Assay performs as well as the gold standard/reference method for the differentiation of Herpes Simplex Virus 1 (HSV-1) and Herpes Simplex Virus 2 (HSV-2) nucleic acids.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

March 26, 2014

QUIDEL CORPORATION
RONALD H. LOLLAR
SENIOR DIRECTOR, CLINICAL AND REGULATORY AFFAIRS
2005 EAST STATE STREET, SUITE 100
ATHENS, OH 45701
USA

Re: K140029
Trade/Device Name: AmpliVue® HSV 1+ 2 Assay
Regulation Number: 21 CFR §866.3305
Regulation Name: Herpes Simplex Virus Nucleic Amplification Assay
Regulatory Class: II
Product Code: OQO
Dated: December 30, 2013
Received: January 6, 2014

Dear Mr. Lollar:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Stephen J. Lovell -S for

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K140029

Device Name: AmpliVue® HSV 1+2 Assay

Indication for Use:

The AmpliVue® HSV 1+2 Assay is an *in vitro* diagnostic test for the direct, qualitative detection and differentiation of Herpes Simplex Virus 1 (HSV-1) and Herpes Simplex Virus 2 (HSV-2) DNA in cutaneous or mucocutaneous lesion specimens from symptomatic patients. The test is intended for use as an aid in diagnosis of HSV infection in symptomatic patients.

***Warning*: The AmpliVue HSV 1+2 Assay is not FDA cleared for use with cerebrospinal fluid (CSF). The assay is not intended for prenatal screening.**

Prescription Use		Over-The-Counter Use
X	AND/OR	
(Part 21 CFR 801 Subpart D)		(21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED

Concurrence of CDRH, Office of In Vitro Diagnostics and Radiological Health (OIR)

Stephen J. Lovell -S
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